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CONTENTS

The British Association for the Advancement of Science:
Progress and Prospects in Chemotherapy: DR. H. H. DALE 185
Devonian Paleontology of Bolivia: PROFESSOR EDWARD W. BERRY 191
American Association for the Advancement of Science:
The Fifth Washington Meeting and Associated Organizations: DR. BURTON E. LIVINGSTON 192
Scientific Events:
The Pan-Pacific Research Institute; The National Geographical Society's China Expedition; The Centennial Celebration of the Rensselaer Polytechnic Institute; Officers of the National Research Council 194
Scientific Notes and News 196
University and Educational Notes 200
Discussion and Correspondence:
New Casts of the Pithecanthropus Remains: DR. ALEŠ HRDLIČKA. *As Students understand it:* PROFESSOR ELLISON A. SMYTH, JR. *The Scientist and an International Language:* CHARLES H. BRIGGS, PROFESSOR ROLAND G. KENT 200
Scientific Apparatus and Methods:
Artificial Cultivation of Free-Living Nematodes: DR. ASA C. CHANDLER 203
Special Articles:
Electric Conductivity of Red Blood Corpuscles: PROFESSOR J. F. MCCLENDON. *Stinging Crystals in Plants:* D. A. HERBERT 204
The Western Society of Soil Management and Plant Nutrition 205
The Western Branch of the American Society of Agronomy 206
Science News x

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PROGRESS AND PROSPECTS IN CHEMOTHERAPY[1]

IN the mind of every physiologist visiting Toronto to-day one recent advance in our science will certainly be uppermost. We rejoice with our colleagues here in a great achievement which has opened new vistas of knowledge to exploration, has brought relief to unmeasured misery, and has turned the eyes of a world, too often careless of such things, in proper gratitude and well-founded hope to this university and its medical school. Insulin, and its still marvelous and mysterious action, have held a prominent place in the interest of many of us, myself included, during the past year or two. In one of our meetings, however, we shall have the opportunity of considering the observations and opinions of many who are now working on its properties and their significance, and among them will be some who were associated with its discovery. I have thought it appropriate, therefore, to ask your attention to-day to some recent developments in a widely different field of investigation. The subject which I have chosen presents points of general physiological and biochemical interest, apart from its immediately practical importance for the treatment of disease. It has, further, in one way, a special appropriateness to this year's meeting of the British Association. For our knowledge of an important group of diseases, caused by the parasitic trypanosomes, which have provided the experimental material for a very large proportion of chemotherapeutic investigations, we are in the largest measure indebted to the pioneer work of the distinguished president of the association, Sir David Bruce.

THE THEORETICAL ORIGIN OF CHEMOTHERAPY

Chemotherapy may be defined as the specific treatment of infections by artificial remedies. The object of those who study it is to find new remedies which will cure or arrest diseases due to infections, not by alleviating the symptoms or invigorating the patient, but by directly and specifically suppressing the infection. Chemotherapy, in this wide sense, is not entirely of recent growth. When the natives of Peru discovered the value in fevers of the cinchona bark, which the Jesuits brought to Europe in the 17th century, they had found a specific remedy for malaria, which is still the best available. Similarly the natives of Brazil had found in ipecacuanha, which reached

[1] From the address of the president of the Section of Physiology of the British Association for the Advancement of Science, Toronto, August, 1924.

Europe shortly after cinchona, a remedy for amoebic dysentery better than any other which our modern systematic and scientific efforts have produced. Modern chemistry, indeed, has separated the alkaloids from these drugs, and has made it possible to identify among them the actively therapeutic constituents; protozoology has revealed the nature of the infections. We know now that cinchona owes its curative action chiefly to quinine and quinidine, and that they act as specific exterminators of the malaria parasites, and not simply as remedies for fevers in general; and we know that ipecacuanha owes its action to emetine and cepheline, and that these act as exterminators of the entamoeba causing tropical dysentery, and not simply as symptomatic remedies for dysenteries of any kind. But chemistry has produced no better remedy for malaria than quinine, or for amoebic dysentery than emetine; and the method by which either of these alkaloids cuts short the infection by a particular parasite, the nature of its specific action, remains a fascinating problem.

The modern development of chemotherapy, as a new department in therapeutic science, claiming the cooperation of parasitologists, microbiologists and synthetic chemists, did not take origin, however, simply from the study of these traditional remedies. It may be regarded rather as an outcome of the study of the natural antibodies. The investigation of these natural antagonists to infection produced a new therapeutic ideal. Not only had they shown themselves to have an intensely specific affinity for the infecting organism of the toxin which caused their production; they were also perfectly harmless to the patient, behaving, in relation to his organism, as normal constituents of his body fluids and tissues. Ehrlich aptly compared them to magic bullets, constrained by a charm to fly straight to their specific objective, and to turn aside from anything else in their path.

Of the artificial remedies, on the other hand, which man had empirically discovered, even of drugs like those just mentioned as being specific for certain infections, the best that could be hoped was that they would eliminate the parasite before they poisoned the patient. And thus, when the limitations of natural immunity were becoming clearer; when it was realized that to certain forms of infection, several of which had proved to be infections by protozoa, the body was unable to produce antibodies of sufficient potency to eliminate the infection and leave the patient immune; the question arose whether, with the new and growing powers afforded by synthetic chemistry, man could not so far rival nature's achievements as to produce in the laboratory substances specifically adapted to unite with and kill the protoplasm of these parasites, as the natural antibodies united with that of others, and to leave the tissues of the patient similarly unaffected. The ideal of this new and systematic chemotherapy, as the imaginative genius of Paul Ehrlich conceived it, was to be the production by synthesis of substances with a powerful specific affinity for and a consequent toxic action on the protoplasm of the parasites, and none for that of the host—of substances, to use Ehrlich's own terminology, which should be maximally parasitotropic and minimally organotropic.

I want to invite your attention to-day to the results which during the last twenty years have been produced under the stimulus of this bold conception; not, indeed, to attempt a survey or summary of all that has been done, but, in the light of a few of the suggestive facts which have emerged, to consider how far this hypothesis has justified itself, and whether it can be accepted as a safe guide to future progress, as it has undoubtedly provided the initiative and working basis for much of what has been accomplished hitherto. Before we deal with some of the actual results obtained, it may be well to consider a little more closely what Ehrlich's working hypothesis involved. The problem was to discover, by chemical synthesis, a compound which, in virtue of its chemical structure, should have a maximal affinity for the protoplasm of a microscopic parasite, such as a trypanosome, and a minimal affinity for that of the host's body cells. These affinities were pictured by Ehrlich, in the terms of his side-chain theory, as determined by certain side-chains of the complex protein molecule, or chemoreceptors, which endowed the protoplasm with specific combining properties. When it is remembered that knowledge of the chemistry of the protoplasm of a trypanosome is almost nil, and that what little we do know suggests that it is very similar to that of our own cells, it will be admitted that the enterprise was one calling for scientific courage and imagination in the highest degree. Complete failure would not have been surprising; the matter for surprise, and for admiration, is that so large a measure of practical success should, at the end of two decades, already claim record.

Trypanosomes and Spirochetes

The Action of Dyes and Analogous Compounds

The investigations leading, in the last few years, to a clear promise, at last, of the successful treatment of the diseases in man and animals due to infections with trypanosomes, had at least two different starting-points, the action of dyes and the action of arsenic. Ehrlich's early interest in the synthetic dyes and his observations of the curiously selective distribution which they often exhibited among the cells and tissues of the body naturally suggested the possibility of finding in this group a substance which would selectively fix itself to the parasite and poison its protoplasm without injuring that of the host. The tech-

nique developed by Laveran and Mesnil, by which a particular strain of trypanosomes could be passed through a series of mice or rats, and produce an infection of standardized type and virulence, enabled the effect of a large selection of dyes to be investigated, with the view of finding one which would favorably influence the infection. A starting-point having been obtained, the resources of synthetic dye production were available to produce an indefinitely long series of derivatives and modifications of the active compound, each to be tested in its turn. In this way Ehrlich and Shiga arrived at a substance which gave experimental promise of curative value, a benzidine dye to which the name "Trypan red" was given.

Two years later, Mesnil and Nicolle, proceeding further along the same path, described an even more favorably active blue toluidine dye, "Trypan blue." This is the only one of the dyes which has hitherto had a genuine practical success in the treatment of a protozoal infection, not indeed by a trypanosome, but by an intracorpuscular parasite of the genus Piroplasma, which infects dogs and cattle. This successful application of Trypan blue to an animal disease has a special interest for us to-day, in that it resulted from the joint labors of last year's president of this section, Professor Nuttall, with a Canadian collaborator, Dr. Hadwen.

We may turn aside at this point to inquire how far the results even of these earlier investigations corresponded with the theory which gave them their impetus. Did these dyes really act by selectively staining and killing the parasites, and leaving the host's cells untouched? The evidence was certainly not in favor of such a view. Ehrlich and Shiga themselves observed that Trypan red, even in relatively high concentrations, was practically innocuous to the trypanosomes outside the body. The trypanosomes, like other cells, were not stained by the dye until they died, and there was no clear evidence that they died sooner in the Trypan-red solution than in ordinary saline. Again, Trypan red cured an infection by the trypanosome of "Mal de Caderas" (*T. equinum*) in the mouse, but not the same infection transferred to the guinea-pig, rat or dog; nor did it cure an infection with the trypanosome of Nagana (*T. brucei*) in mice. Now, to explain such a difference by stating that the affinity of Trypan red for *Trypanosoma equinum* was much higher than its affinity for the tissues of the mouse, but not than its affinity for those of the rat, would be merely to restate, in terms of the theory, the observed fact that the mouse was cured while the rat was not; and the lack of direct affinity for the dye shown by trypanosomes outside the body made such an interpretation in any case unsatisfactory. One point, however, appeared very significant, and it is met repeatedly in studying the action of effectively chemotherapeutic substances, namely, that the trypanosomes treated with the dye *in vitro*, though neither obviously stained nor visibly harmed, had lost their power of infection, and died out promptly if introduced into the body of a mouse. Under such conditions only minimal traces of the dye are introduced into the animal, and we are left with a series of alternative possibilities. It is possible that sufficient dye has been taken up by the trypanosomes to kill them eventually, the period of survival *in vitro* being inadequate to display its action; or that Trypan red is converted by the influence of the body fluids and tissues into something which is effectively lethal for the parasite; or, again, that the effect of the drug is not directly to kill the trypanosomes, but, leaving their individual vitality and motility unimpaired, so to modify them that they have lost the power of rapidly reproducing themselves and invading the fluids and tissues of the mouse's body—in other words, have lost that complex of adjustments to the various factors of the host's natural resistance which we crudely summarize as "virulence." Such possibilities involve either storage or modification of the dye by the host's tissues or their essential cooperation in its curative effect.

One other active dye must be mentioned as providing the link with a recent, most important advance. Mesnil and Nicolle in 1906 made some promising experiments with a dye, Afridol violet, which differed from any previously tested in that its central nucleus was diamino-diphenyl-urea. From this time onwards there was no further public indication of progress along these lines until 1920, when Händel and Joetten published the results obtained with a remarkable substance which, as the result of some fifteen years of continuous work by their scientific staff, had been introduced by the great dye and chemical firm of Bayer. This substance, which is not a dye, but the colorless, water-soluble salt of a complex sulphonic acid, has hitherto been known as Bayer "205," and, for reasons which need not concern us, the firm decided not to publish its formula. To students of their patent specifications, however, it seemed pretty certain that it would prove to be one of a long series of compounds, formed of chains of aminobenzoyl radicles, united by amide linkages, with a central urea linkage, like the dye last mentioned, and terminal naphthylamine sulphonic acid groupings. A number of these substances, having no diazo-linkages, were not dyes, but there was no indication as to which constitution, out of an immense number possible, would prove to be that of the remarkable substance numbered "205." There is a reasonable probability that its identity has now been settled by the recent work of Fourneau and his coworkers in the Pasteur Insti-

tute, who made and investigated an extensive series of compounds of this general type, and found one, which they numbered "309," which conspicuously excelled all others, even those closely related to it, in the favorable ratio which it displayed between a just toxic dose and that which caused a trypanosome infection in mice to disappear. As in the case of "205," the ratio, the "chemotherapeutic index" of Ehrlich, was found by Fourneau in some experiments with his compounds to be well over 100. At least it may be said that, if M. Fourneau has not identified Bayer "205," he has discovered another compound having very similar and probably as valuable properties.

The most remarkable property of "205" is the long persistence of its effect. A dose injected into a mouse, a rabbit or a rat will not only free the animal, if already infected, from trypanosomes in a few days, but will also render it resistant to such infection for a period of weeks or even months. During that period its serum, or extracts from certain of its organs, exhibit a curative action if injected into another animal infected with trypanosomes.

Though there seems no reason to doubt that this substance has cured a number of cases of African sleeping-sickness in man, even some in which the disease was well advanced and in which all previously known remedies had failed, the mode of its action still presents a number of attractive obscurities. Like many other remedies which are experimentally efficient when injected into the infected animal, it has little or no obvious action when directly applied to trypanosomes *in vitro*. The paradox is, perhaps, less than usually significant in this case, since the action in the animal is delayed, a period of a few days elapsing before the trypanosomes begin to disappear from the blood. We might suppose that the action is too slow to be recognized during the period of survival of the parasites outside the body, or that it affects not the individual vitality of the trypanosomes, but their power of reproducing themselves. The latter idea is supported, as in other cases, by the fact that trypanosomes treated with the drug *in vitro*, or taken from an injected animal before the curative effect has become manifest, fail to infect another animal. It is contradicted, however, by the observation that the trypanosomes, just before the curative action begins, show not a depression, but a stimulation of reproductive activity, division forms becoming abnormally common. Is it that during or immediately after division the parasites become specially liable to the action of the drug? It may be so; but one thing seems perfectly clear, namely, that the action is a very complex one, involving the cooperation, in some way, of the host. For here again it is found that the curative action, on infections by the same strain of trypanosomes, varies enormously with the species infected, a mouse being cured with ease, an ox or a horse with difficulty or not at all. A curious fact is that the rapidly progressive and fatal infections produced in mice by certain pathogenic trypanosomes are easily and certainly cured, while the apparently harmless natural infection, seen in many wild rats, by *T. lewisi* is not affected at all. Then there are some curious records of treatment in man, in which the symptoms of sleeping-sickness have disappeared, but the trypanosomes are still found in the cerebro-spinal fluid, suggesting that, though the parasites have not been killed, they have lost their virulence and their power of invading the brain substance.

The features of the action of this remedy, however, which have most interest for the physiologist and the biochemist are those related to the long persistence of its effect. "205" has a large molecule, but it is extremely soluble in water and diffusible through collodion membranes. How, in such circumstances, can we explain the persistence of its sterilizing and prophylactic action for months after an injection? At first sight one is tempted to regard it as incredible that a substance with these properties should persist in the body for such a period, and to suggest that the action must be due to its stimulation of the body to form its own protective substances. This possibility, however, seems to be excluded by the fact that the serum of the protected animal does not lose its curative properties if heated. On the other hand, there have recently appeared, some of them only in preliminary abstract, a series of highly suggestive observations, indicating that "205" has properties of entering into a combination of some kind with the serum proteins. After standing for an hour or two in serum, "205" no longer passes into an ultra-filtrate through collodion, and if the proteins are coagulated by heat is not to be found in the filtrate. The proteins of the blood, moreover, are stated to lose many of their characteristic properties by entering into this combination, the blood losing its normal power of clotting and the serum proteins not being precipitated by mercury salts or tannin.

It would be both useless and presumptuous for a mere onlooker to speculate in detail on the significance, for the curative action of "205," of properties which are only now beginning to be investigated. One conclusion, however, I think we are entitled to draw. It is sufficiently evident that here is no question of a substance curing simply on account of its affinity for parasites and lack of affinity for the host's tissues. What direct action on the parasite "205" itself may possess has still to be demonstrated; we may feel reasonably certain, on the other hand, that its affinities for the constituents of the host's blood and tissues play an important part in its remarkable and peculiar curative properties.

Derivatives of Arsenic

In the case of the other series of investigations which I mentioned, that dealing with the organic derivatives of arsenic, we find again many difficulties, in the way of the simple theory, of a cure due to distribution by chemical affinities. None of the compounds of this series, which have reached practical trial and success in the treatment of spirochetal or trypanosomal infections, atoxyl, salvarsan or tryparsamide, has a directly lethal action on the parasites in dilutions at all comparable to those which can be safely and effectively produced in the body of the host. The paradox of this direct inertness of atoxyl, the starting-point of the series, seemed to be explained when Ehrlich showed that its reduction to the corresponding arsenoxide produced a substance with an intense directly lethal action on trypanosomes. Similarly, the partial oxidation of salvarsan, to the corresponding arsenoxide, produced a substance having the intensely lethal action on spirochetes or trypanosomes *in vitro,* which salvarsan itself conspicuously and paradoxically lacked. In these cases, we may make the supposition, which Voegtlin and his coworkers, especially, have recently supported by detailed evidence, that the reduction or oxidation effected by contact with the tissues is the essential preliminary to the curative action; a supposition which, it will be noted, again introduces the host as an essential participant in the cure. The fact that the administration of these relatively inactive predecessors is therapeutically more effective than the injection of the directly active oxides derived from them would then be explained on the assumption that the slow liberation of these latter in the body, at a rate which never produces a high concentration, provides the optimum condition for their persistent action on the parasites without danger to the host. This slow and persistent liberation of the directly active substance would be favored by the physical properties of salvarsan, which at the reaction of the body is practically insoluble, and must be rapidly deposited after injection.

In their recent work on the action of Tryparsamide, the compound prepared by Jacobs and Heidelberger at the Rockefeller Institute which has shared with Bayer "205" the credit of making the eventual conquest of African sleeping-sickness a hopeful possibility, Brown and Pearce find it necessary to introduce yet other considerations to explain its effects. Tested by Ehrlich's therapeutic index—the ratio between the lowest curative and the highest non-toxic dose—it gives a relatively unfavorable figure. Brown and Pearce practically abandon the attempt to account for its action on the supposition that it directly kills the parasites and attribute its value largely to its power of penetrating easily into the tissues and reinforcing there the processes of natural resistance.

Action of Bismuth

Another conception of the mode of action of these arsenical remedies, also involving a direct participation in the host's tissues, was put forward by Levaditi. He found that from atoxyl a directly parasiticidal preparation could be obtained by incubating it with an emulsion of fresh liver substance. As the first step, therefore, in the curative action of atoxyl, he postulated a combination of its reduction product with some constituent of the liver or other tissue, giving rise to the essential curative complex, which he named "trypanotoxyl." Levaditi's observations were explained by Ehrlich and Roehl as due simply to the reducing action of the liver substance on atoxyl; but it would be difficult to apply this explanation to the quite recently published observations by Levaditi and his colleagues on the mode of action of bismuth in curing spirochetal infections. A sodium potassium bismuthyl tartrate—a bismuth analogue of tartar emetic—had been found to have valuable curative properties in syphilis and other spirochetal infections. Later, various other bismuth salts, bismuth suboxide and even finely divided metallic bismuth were found to produce similar effects. According to Levaditi and Nicolau, these preparations have, by themselves, a relatively weak action, or none at all, on the spirochetes outside the body. If they are mixed, however, with a cell-free extract of liver, which is itself harmless to spirochetes, the mixture, after incubation, acquires a potent spirocheticidal action. The possibility of a mere reducing action of the liver extract seems here to be excluded, since bismuthous oxide or metallic bismuth itself yields a spirocheticidal mixture, containing Levaditi's hypothetical "bismoxyl," when incubated with the liver extract. If these observations are confirmed, there will be a strong indication that some cell-constituent enters into the composition of or is essential to the formation of the directly active substance from any of the derivatives of arsenic, antimony or bismuth, as a preliminary to its action on an infection due to a trypanosome or a spirochete. Again we have evidence of an organotropic property of the remedy, as an essential condition of its activity.

Resistant Strains of Trypanosomes

In the phenomena of the acquisition of resistance, by a strain of infecting trypanosomes to a particular curative drug, discovered and largely worked out in Ehrlich's laboratory, we meet again with facts which can only with the greatest difficulty be reconciled with the assumption that the drug directly attacks the parasites. It was found, for example, that if a mouse infected with trypanosomes received an incompletely effective series of doses of atoxyl, the trypanosomes appearing in the blood at each relapse were more

and more resistant to the drug, unitl they could not be caused to disappear by any dose of atoxyl which the mouse would tolerate. The strain, having once acquired this resistance, would retain it, on passage through an indefinitely long series of mice, without further treatment. Mesnil and Brimont, however, made the remarkable observation that, if the strain of trypanosomes was transferred to a rat, it immediately became in that animal susceptible again to treatment with atoxyl, remained so as long as it was kept in rats, to reacquire its old resistance to atoxyl as soon as it was retransferred to mice. Such a fact seems to be not at all explicable on the theory that the directly active agent, to which the trypanosome becomes resistant, is a mere reduction product of atoxyl; it is much more easily reconciled with a mechanism such as that described by Levaditi, in which a constituent of the host's tissues enters into the formation of the trypanocidal substance. We can imagine the trypanosome becoming immune to Levaditi's mouse-trypanotoxyl, and remaining susceptible to the corresponding rat-product.

The whole question of this acquired resistance of the parasites to the action of curative drugs bristles with points of difficulty and interest. Ehrlich attributed the sensitiveness of the parasite, for a particular curative agent, to the possession by its protoplasmic molecule of a special form of side chain, or "chemoreceptor," which determined its affinity for that agent. When the trypanosome became resistant, it was simple to suppose that it did so by losing the appropriate chemoreceptors; an atoxyl-resistant trypanosome, for example, had lost its atoxyl receptors. Apart from the objections already mentioned, this conception met a new difficulty, when in Ehrlich's laboratory it was found that the resistance was by no means as rigidly specific as it had first appeared to be. Not only imperfect treatment with atoxyl, but treatment with a particular group of dyes, having no kind of chemical relation to it, was found to produce a race of trypanosomes resistant to atoxyl and to other arsenical derivatives. To suggest that the chemoreceptors for arsenic and for these dyes are identical is merely to restate the fact of this reciprocal action in terms having no definite meaning. Obviously no more precise conception as to its significance can be formed until we know something more of the conditions on which resistance and susceptibility depend. A recent suggestion by Voegtlin has interest in making, at least, an attempt at interpretation in more definite biochemical terms. Voegtlin and his coworkers point out that arsenious oxide and its derivatives readily combine with substances containing a sulphydrile grouping and find that the toxic action of the organic arsenoxides on trypanosome and mammal alike is depressed by the simultaneous injection of excess of various sulphydrile compounds.

Suggested Reaction of an Arsenoxide with a Sulphydrile Compound

The work of Hopkins, showing the importance of one such sulphydrile compound, reduced glutathione, in the hydrolytic oxidation-reduction processes of the cell, suggests to Voegtlin that a combination with such groups and consequent suppression of this vital function may explain the toxic and curative actions of the arsenical derivatives and that a formation by the trypanosome of the sulphydrile compound, in excess of its vital need, may be the basis of acquired resistance. If certain dyes similarly affect this cellular oxidation system, the production under their influence of strains of trypanosomes resistant to arsenic would also be explained. So stated the suggestion leaves many aspects of the problem still unconsidered; but it may at least be allowed the merit of an attempt to interpret the action of these drugs in terms of known biochemical facts.

Conclusion

We have considered but a few examples of the directions in which chemotherapeutic investigation has proved practically fruitful, including some in which it shows, at the moment, the most hopeful signs of progress. If one considers any one group of investigations by itself, one may easily feel, at the same time, elated by the practical success obtained, in the cure of some infection which, but a few years ago, seemed beyond the reach of treatment, and depressed by the disharmony between the results of experiment and the theoretical conceptions, hitherto available, of the nature of the chemotherapeutic process. Some of the most notable practical triumphs in this field have resulted not from experimental investigations based on theory but from an almost empirical trial on human patients suffering from one type of infection of a remedy which had experimentally shown promising results in infections of a different and sometimes of a widely different type. The partial success of tartar emetic in trypanosome infections might have justified a hope that it would have some effect in kala-azar but hardly a prediction of its really remarkable efficacy in that previously intractable form of infection. Still less would it have justified expectation of the brilliant success of this same drug in infections by the Schistosoma or Bilharzia-worm, which but recently seemed almost beyond the hope of any kind of treatment. With such instances in mind, one might, but a year or two ago, have been tempted to suggest that the attempts at theoretical investigation of the intimate mechanism of the chemotherapeutic process had contributed little to the practical achievements, and that a reasonably intelligent empiricism was still the safest guide. I do not think that the suggestion would even then have been defensible, and it would assuredly have been stultified by the results

of the past few years. Patient, systematic exploration, by routes of which the initial sections were already mapped in the early days of chemotherapy, has in these recent years again led to results of major importance, both for practical therapeutics and for the theoretical basis of future advance. That the original theoretical framework begins to show itself inadequate for the expanding fabric is good reason for its reconstruction; but we may well beware of hasty and wholesale rejection, remembering that it served the early builders well. I think that it is especially encouraging to note that, though, in the action of almost every remedy which has proved its value in the specific cure of infection, there are features which can not be interpreted by a strict application of Ehrlich's distribution hypothesis, the discrepancies begin to show a new congruity among themselves. Repeatedly we find phenomena which point to the need of modifying the theoretical structure in the same direction. The conception of a remedy not killing the parasites immediately, but modifying their virulence, or lowering their resistance to the body's natural defences; of a remedy not acting as such, but in virtue of the formation from it in the body of some directly toxic product, either by a modification of its structure or by its union with some tissue constituent; of an affinity of the remedy for certain cells of the host's body, leading to the formation of a depot from which, in long persistent, never dangerous concentration, the curative substance is slowly released; all these conceptions present themselves, again and again, as necessary for our present rationalization of the effects observed. It can hardly be doubted that they will potently influence the methods by which, in the immediate future, new and still better specific remedies are sought. But though our practical aim, in relation to the affinities of a remedy for the parasite and for the host's tissues, may be radically changed, the meaning of these specific affinities, so delicately adjusted to a precise molecular pattern, remains dark. Ehrlich's chemoreceptors may no longer satisfy us, but we have nothing equally definite to replace them. I have endeavored to indicate what seem to me hopeful signs of new contacts between biochemistry and chemotherapy. There is promise, in another direction, that at least some aspects of the problem of immune specificity are being brought within the scope of strictly chemical investigation, as in the recent work of Avery and Heidelberger, on the constituent of a pneumococcus which combines with the specific precipitin. As in Ehrlich's pioneer work in chemotherapy, it can hardly be doubted that an increased understanding of the meaning of immune specificity, which but a short while ago might have seemed hopelessly beyond the range of attack by chemical weapons, will still influence ideas and help to shape the course of further investigations on the chemotherapeutic process. As the biological complexity of the problem is realized, it becomes increasingly a matter for wonder and admiration that so much of practical value has already been achieved—the treatment of the spirochetal infections, syphilis, yaws and relapsing fever, revolutionized; Leishmania infections, kala-azar and Baghdad boil and Bilharzia infections which crippled the health of whole populations in countries such as Egypt, now made definitely curable; trypanosome infections, such as the deadly African sleeping-sickness, after years of alternating promise and disappointments, brought now at last within the range of effective treatment. And if such results have already been attained, in a period during which practice has often and inevitably outrun theory, we may well be hopeful for a future in which fuller understanding should make for more orderly progress.

H. H. DALE

DEVONIAN PALEONTOLOGY OF BOLIVIA

No geological system in South America has been so well explored as has the Devonian. The bead-roll of eminent contributors to the elucidation of South American Devonian paleontology commences with the name of d'Orbigny in 1842 and includes longer or shorter contributions by Salter (1861), Rathbun (1874, 1878), Hartt (1875), A. Ulrich (1893), von Ammon (1893), Katzer (1896–1898), Kayser (1897, 1900), Haug (1905), Thomas (1905), Newton (1906), and Knod (1908). John M. Clarke, whose labors in this field cover nearly a quarter of a century (1890–1913), and culminated in his magnificent monograph published in 1913, in which the whole field was covered in his characteristic masterly way, has contributed more than any one else to this subject.

The eastern South American Devonian has, on the whole, received more attention and more thorough treatment than that of the Andean region, although Devonian beds outcrop for hundreds of miles along the medial extent of the Andean system. The Devonian is well represented and fairly fossiliferous in Bolivia, in which general region d'Orbigny first collected Devonian fossils in South America, but these Devonian faunas have not heretofore received the exhaustive treatment that has been devoted to those of Brazil.

Last year there appeared in the Annales de Paléontologie a monograph of the Devonian of Bolivia by Roman Kozlowski,[1] who spent six years in Bolivia, first as a professor and subsequently as director of the School of Mines at Oruro. In this work there are described 138 different forms, making the Bolivian

[1] Kozlowski, R., "Faune Dévonienne de bolivie." Ann. Paléont., tome xii, 112 pp., 10 pls., 1923.

fauna the largest known from South America, that from Paraná, for example, consisting of 73 species. This fauna comprises 33 trilobites, 9 cephalopods, 5 conularias, 7 pterapods, 15 gastropods, 26 pelecypods, 33 brachiopods, 3 echinoderms, 3 bryozoa and 4 corals. The few corals, bryozoa and crinoids; the reduced number of brachiopods, and the great abundance of pelecypods emphasize the prevailing muddy environment during Devonian time in Bolivia.

The sub-divisions of the Bolivian Devonian are geographic rather than stratigraphic, although Kozlowski believes the succession given below as probable: At the base are the shales of the Cordillera Real, as at Araca, and these are correlated with the North American Helderberg. Above this lies the Icla formation, consisting of the *Rensselaria knodi* sandstone, the Conularia shales and the Huamampampa sandstone. These are collectively correlated with the Oriskany of North America, the Maecurú sandstone of Pará, the Devonian of Paraná, Matto Grosso, the Argentina, Falkland Islands and the Bokkeveld beds of Africa.

Above the Icla formation is the Sicasica formation of the Altaplanicie, which consists of the lower fossiliferous shales, the *Homalonotus dekayi* shales and the upper barren sandstone. These are correlated with the Ereré sandstone of Pará, and with the middle Devonian of North America, and possibly extending upward into the upper Devonian.

The austral character of the Devonian faunas of South America, emphasized by Clarke, are, in Bolivia, shown chiefly by the Phacopidae. Paraná and Africa show the largest number of identical forms, and Africa has twice as many as Pará. Kozlowski is inclined to think that the barrier that prevented intercommunication between Bolivia and Pará was water too deep to permit the interchange of shallow water faunas rather than a land barrier, and this implies that such a deep water barrier was lacking at that time between South Africa and Bolivia.

Kozlowski identifies a considerable number of North American species in the Bolivian Devonian. These occur for the most part in the supposed younger Devonian Sicasica formation, and include such forms as *Homalonotus dekayi, Orthoceras constrictum, Nuculites oblongatus, Tropidoleptus carinatus, Vitulina pustulosa;* and closely related forms of Lophospira, Ambocoelia, Liorhynchus and Spirifer. From this he concludes that the means of intercommunication between North America and Bolivia were easier at that time than in the earlier Devonian. We have compared these with material in the Hopkins collections from Bolivia, and with North American specimens, and believe that such an identity is not established in all cases, but this is a question to be decided by more material and by someone better versed in Devonian paleontology than the reviewer.

Kozlowski's memoir is a most complete and scholarly contribution. His adequate and well-executed illustrations amply supply the deficient and poor illustrations of Bolivian material in the works of Ulrich and Knod. The work is a most welcome contribution to the paleontology of South America, and lays a secure basis for future studies of the Andean Devonian.

EDWARD W. BERRY
THE JOHNS HOPKINS UNIVERSITY

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

PREPARATIONS FOR THE FIFTH WASHINGTON MEETING AND ASSOCIATED ORGANIZATIONS

THE local committees in charge of preparations for the approaching Washington meeting of scientists (December 29, 1924, to January 3, 1925) have been organized as follows:

The Local Committee for the Fifth Washington Meeting

William Mather Lewis, president of George Washington University, *chairman.*

C. G. Abbot, assistant secretary, Smithsonian Institution.

Gilbert H. Grosvenor, president of the National Geographic Society.

Vernon Kellogg, permanent secretary of the National Research Council.

John C. Merriam, president of the Carnegie Institution of Washington.

David White, home secretary of the National Academy of Sciences, and senior geologist, U. S. Geological Survey.

The Committee on Special Arrangements for the Fifth Washington Meeting

Walter M. Gilbert, administrative secretary, Carnegie Institution of Washington, *chairman.*

Albert L. Barrows, assistant secretary, National Research Council.

Paul Brockett, assistant secretary, National Academy of Sciences.

Austin H. Clark, curator, Division of Echinoderms, U. S. National Museum.

Hugh Miller, dean of engineering, George Washington University.

W. J. Showalter, associate editor, National Geographic Society.

Chairmen of Subcommittees

Albert L. Barrows, Hotels.

Paul Brockett, Transportation.

Austin H. Clark, Publicity.
Walter M. Gilbert, Finances.
Hugh Miller, Meeting Places.
W. J. Showalter, Exhibition.

Local Representatives for the Sections

Section A (Mathematics). Howard L. Hodgkins, George Washington University.

Section B (Physics). Lyman J. Briggs, 3208 Newark street.

Section C (Chemistry). R. S. McBride, Colorado Building.

Section D (Astronomy). W. S. Eichelberger, U. S. Naval Observatory.

Section E (Geology and Geography). W. C. Mendenhall, U. S. Geological Survey.

Section F (Zoological Sciences). Paul D. Bartsch, U. S. National Museum.

Section G (Botanical Sciences). R. F. Griggs, George Washington University.

Section H (Anthropology). J. Walter Fewkes, Smithsonian Institution.

Section I (Psychology). William C. Ruediger, George Washington University.

Section K (Social and Economic Sciences). Frederick L. Hoffman, Babson Institute, Wellesley Hills, Mass.

Section L (Historical and Philological Sciences). Frederick E. Brasch, Department of Terrestrial Magnetism, Carnegie Institution of Washington.

Section M (Engineering). William Bowie, U. S. Coast and Geodetic Survey.

Section N (Medical Sciences). Carl Voegtlin, Hygienic Laboratory.

Section O (Agriculture). Karl F. Kellerman, Bureau of Plant Industry.

Section Q (Education). C. R. Mann, 26 Jackson Place.

The following named organizations have thus far intimated their intention to hold meetings at Washington in convocation week, in conjunction with the association. The name and address of the secretary follows the name of the organization. Organizations marked with an asterisk are officially affiliated with the association:

*American Mathematical Society. R. G. D. Richardson, Brown University, Providence, R. I.

*Mathematical Association of America. W. D. Cairns, Oberlin, Ohio.

Pi Mu Epsilon Mathematical Fraternity. E. D. Roe, Jr., 123 W. Ostrander Ave., Syracuse, N. Y.

*American Physical Society. Harold W. Webb, Columbia University, New York, N. Y.

*American Meteorological Society. Charles F. Brooks, Clark University, Worcester, Mass.

*American Astronomical Society. Joel Stebbins, Washburn Observatory, Madison, Wis.

*Association of American Geographers. Charles C. Colby, University of Chicago, Chicago, Ill.

National Council of Geography Teachers. Geo. J. Miller, Mankato, Minn.

*American Society of Zoologists. W. C. Allee, University of Chicago, Chicago, Ill.

*Entomological Society of America. Clell Lee Metcalf, University of Illinois, Urbana, Ill.

*American Association of Economic Entomologists. C. W. Collins, Melrose Highlands, Mass.

*Botanical Society of America. I. F. Lewis, University of Virginia, University, Va.

*American Phytopathological Society. R. J. Haskell, U. S. Department of Agriculture, Washington, D. C.

American Society of Plant Physiologists. R. B. Harvey, University of Minnesota, Minneapolis, Minn.

*American Society of Naturalists. A. F. Shull, University of Michigan, Ann Arbor, Mich.

*Ecological Society of America. A. O. Weese, James Millikin University, Decatur, Ill.

*American Microscopical Society. Paul S. Welch, University of Michigan, Ann Arbor, Mich.

*American Anthropological Association. A. V. Kidder, Phillips Academy, Andover, Mass.

American Folk-Lore Society. Gladys A. Reichard, Barnard College, Columbia University, New York, N. Y.

*American Psychological Association. John E. Anderson, Drawer 13, Yale Station, New Haven, Conn.

Metric Association. Howard Richards, Jr., 156 Fifth Ave., New York, N. Y.

American Physiological Society. Walter K. Meek, University of Wisconsin, Madison, Wis.

*Society of American Bacteriologists. J. M. Sherman, Cornell University, Ithaca, N. Y.

American Society for Pharmacology and Experimental Therapeutics. Edgar D. Brown, University of Minnesota, Minneapolis, Minn.

American Society of Biological Chemists. Wright Wilson, University of Pennsylvania, Philadelphia, Pa.

American Society for Experimental Pathology. E. B. Krumbhaar, Chestnut Hill, Philadelphia, Pa.

*American Society for Horticultural Science. C. P. Close, College Park, Maryland.

Association of Official Seed Analysts. A. L. Stone, University of Wisconsin, Madison, Wis.

Potato Association of America. William Stuart, U. S. Department of Agriculture, Washington, D. C.

Phi Delta Kappa Fraternity. Clayton R. Wise, 13319 E. Sixth St., E. C. Cleveland, Ohio.

*Society of Sigma Xi. Edward Ellery, Union College. Schenectady, N. Y.

*American Association of University Professors. H W. Tyler, 222 Charles River Road, Cambridge, Mass.

*Gamma Alpha Graduate Scientific Fraternity. L. M. Hutchins, U. S. Bureau of Plant Industry, Washington, D. C.

The local arrangements for sections and for associated organizations are in charge of the local section

representatives named above, who are in close touch with the Committee on Special Arrangements. Secretaries of associated organizations and of sections of the association are asked to correspond with the local representatives of their respective sections when taking up arrangements for hotel headquarters, dinners, meeting places, lanterns, etc. For organizations that are not specially related to any section of the association these arrangements are to be made through correspondence with the assistant secretary, Dr. Francis D. Murnaghan, who is to be addressed at the Washington office.

The general hotel headquarters for the meeting will be the New Willard Hotel, Pennsylvania Avenue and Fourteenth Street N. W. It is probable that some associated societies will have other hotel headquarters. A list of Washington hotels and their prices will be published later in SCIENCE and in the Preliminary Announcement of the meeting, which will be sent, as usual, to all members on or before December 1.

Reduced railway rates on the certificate plan have been granted to those attending the Washington meeting from all parts of the United States and from points in Canada, east of and including Armstrong, Fort William and Sault Ste. Marie, Ont. The certificate plan is the same as that followed for recent meetings.

It is hoped that the publicity feature of the Washington meeting will be handled even more efficiently than has been done at recent meetings of the association. The newspapers are prepared to give much space to science, and the association will do its best to furnish facilities by which representatives of the press may readily secure reliable information and may interview the men of science on their work. The subcommittee on publicity will again have the helpful cooperation of Science Service, as in recent years.

All persons who are to read papers or present addresses at the Washington meeting will aid the advance and the popularization of science very much if they will be sure to prepare *two copies* of a summary or abstract of each paper, sending one to Austin H. Clark, publicity chairman, U. S. National Museum, and the other to the editor of Science Service, Building of the National Academy of Sciences, Washington, D. C. These summaries should be sent in as early as possible. We hope for advanced summaries of all the papers given this year.

The member who made possible the thousand-dollar prize awarded at the Cincinnati meeting has very generously provided funds for a similar prize to be awarded at the fifth Washington meeting, and at the four subsequent annual meetings. The Washington prize will be awarded to the author of a noteworthy contribution to the advancement of science, presented in the programs of the association and associated organizations.

The fifth Washington meeting will be large and well attended, and plans are being made for many program features that will well represent the present status of American scientific work and scientific thought. An exhibition of new scientific apparatus, methods, books and products is being arranged. It is hoped that individuals as well as firms will exhibit. General plans for the exhibition are in charge of Dr. Chas. A. Shull, Botany Building, the University of Chicago. Prospective exhibitors are asked to correspond with him in this regard.

The opening session of the fifth Washington meeting will occur on the evening of Monday, December 29, at which Dr. Charles D. Walcott, secretary of the Smithsonian Institution, will deliver the retiring presidential address. It is hoped that the President of the United States will address the association and associated societies at the oppening session. On Tuesday evening, December 30, will occur the usual joint session of the American Association and the Society of Sigma Xi, and the session by Dr. Frederick Fuller Russell, general director of the International Health Board. On Wednesday evening, December 31, a general session will be addressed by the eminent British astronomer, Arthur Stanley Eddington, Plumian professor of astronomy in Cambridge University and director of the Cambridge Observatory. His subject will be "Relativity."

BURTON E. LIVINGSTON,
Permanent Secretary.

SCIENTIFIC EVENTS

THE PAN-PACIFIC RESEARCH INSTITUTE

THE Castle home, in Honolulu, with four acres of surrounding land, is to become the home of a Pan-Pacific scientific research institute. The property is to be used solely as a college of graduates. The assistant students will, it is expected, attend the University of Hawaii, where they will take their degrees.

The gift will be used as the nucleus of the Pan-Pacific University, for which a charter was granted some years ago. This will be a graduate university chiefly for research work. Probably a Pan-Pacific research college or institute will be granted a license by the incorporators of the Pan-Pacific University to begin work at once with a trusteeship of five scientists of Pacific races who will proceed with the organization of the research institute.

The chief work of the Pan-Pacific Research Institute will be along lines of research study of food resources of Pacific lands and of the ocean itself. It will be entirely a Pan-Pacific institute connected with no other body but cooperating with kindred bodies in all Pacific lands. It will be neither American, Ha-

waiian nor Japanese, but governed by scientists from all Pacific regions.

Conferences are being held with the heads of several delegations already there from Pacific lands, and cable invitations have been sent to others to hurry on and take part in the deliberations as to the work the institute shall undertake for the peoples of the Pacific area.

The scientists who have been for some months planning the Pan-Pacific Research Institute will make a report at the coming conference, and it is understood that the institute will begin operations at once, offering its services for the years of follow-up work needed in making the resolutions passed at the coming conference effective.

The Castle home is one of the largest in Honolulu, amply housing two score workers, with one extra outbuilding almost as large, which is excellently planned for laboratory uses. In addition there are several smaller buildings, four acres of ground, a complete set of concrete tanks and water supply sufficient for laboratory purposes. The buildings could house, beside the permanent staff, some forty visiting research scientists.

According to press dispatches, Dr. David Starr Jordan, chancellor emeritus of Stanford University, has tentatively accepted the directorship of the institute.

THE NATIONAL GEOGRAPHIC SOCIETY'S CHINA EXPEDITION

JOSEPH F. ROCK, head of the National Geographic Society's expedition into Yunnan, southwestern Szechuan and southeastern Tibet, has just returned to this country after eighteen months in the field and reported the finding of aboriginal tribes in China practicing religious ceremonies which existed before Buddhism was introduced into either China or Tibet.

Mr. Rock found a blight-resistant chestnut tree, made observations over considerable unmapped territory, traversed a hitherto unexplored Yangtze River gorge which in places is much deeper than the Grand Canyon of the Colorado, and brought back important plant and bird collections.

The expedition's collection of herbarium specimens approximated some 60,000 sheets representing some 12,000 numbers. These plants were collected in the extreme northwest of Yunnan, Tsarong, southeastern Tibet, the independent Lama Kingdom of Mili and also in eastern Yunnan. The birds collected number about 1,600. These have been carefully skinned and prepared and labeled, and scientific data accompanies each specimen. They are from regions where few collections had previously been made. The collection contains land and water birds and in addition a few hundred mammals. The birds and mammals will be presented to the Smithsonian Institution as a gift from the National Geographic Society.

Chestnuts of apparently immune species have been presented to the Department of Agriculture, Bureau of Plant Industry. In addition a fine set of coniferous plants such as firs, spruces, hemlocks, pines and junipers were turned over to the Department of Agriculture. A large collection of seeds of rhododendrons also was forwarded to the department. Seeds of 493 kinds of rhododendron were sent to the department, by far the largest single introduction ever made into this country.

Mr. Rock's chestnuts include several species heretofore unknown to the horticultural world and perhaps even to botanical science. The chestnut introduction is of great interest to the tanning industry which has depended upon chestnut to a great extent and has recently faced the possibility of this supply being destroyed through the ravages of blight.

Mr. Rock's plant specimens were forwarded from time to time and rhododendrons also have been sent to Kew Gardens, to Edinburgh, Scotland, and to the Honorable Vicary Gibbs and A. K. Bulley, both of England, amateurs who specialize in these plants and whose collections are famous. In the United States some of them already have been planted at Golden Gate Park in San Francisco, in the Puget Sound Region and along the eastern seaboard. Further distributions are to be made in this country.

Gentians, primroses and other alpine plants, of which sets were sent by Mr. Rock, will be of great interest to gardeners in this country and in Europe. Some of these sets also have been sent to botanical gardens and plantsmen in Great Britain.

THE CENTENNIAL CELEBRATION OF THE RENSSELAER POLYTECHNIC INSTITUTE

THE centennial celebration of the Rensselaer Polytechnic Institute, the oldest college of science and engineering in any English-speaking country, will take place at Troy, New York, on October 3 and 4. There will be present official delegates from educational institutions, scientific organizations and engineering societies throughout the world as well as from each alumni association and from each class since 1857. The program as thus far arranged is as follows:

OCTOBER 3

Morning: Academic Procession.

Convocation. Addresses by:

Hon. Herbert Hoover, secretary of commerce of the United States.

Hon. Alfred E. Smith, governor of the State of New York.

Hon. Harry E. Clinton, mayor of Troy.

President Sir Charles Langbridge Morgan, of the Institute of Civil Engineers of Great Britain.

President Henri Abraham, of the Society of Electrical Engineers of France.

President Luigi Luiggi, of the Society of Civil Engineers of Italy.

Honorary President Roberto Gayol, of the Society of Engineers of Mexico.

President Arthur Surveyer, of the Engineering Institute of Canada.

Afternoon: Unveiling of Tablets.

1. On the site of the old main building, destroyed by fire in 1904. Address by Hon. Seymour van Santvoord, of Troy, and Mrs. James Carroll Frazer, of Washington, a lineal descendant of Stephen Van Rensselaer, founder of the institute.
2. In the Carnegie Building in memory of S. Wells Williams ('32), first professor of Chinese and oriental literature in Yale University. Address by His Excellency, Dr. S. K. Alfred Sze, Chinese Minister to the United States.

Inspection of laboratories.

Evening: Dinner in the State Armory. Addresses by:

President Livingston Farrand, of Cornell University.

Director Joseph H. Odell, of the Service Citizens of Delaware, and another distinguished speaker.

Pageant on the campus illustrating scenes in the history of science and engineering during the last hundred years.

OCTOBER 4

Morning: Convocation. Addresses by:

President Angell, of Yale University.

President Birge, of the University of Wisconsin.

President Stratton, of the Massachusetts Institute of Technology.

President Grunsky, of the American Society of Civil Engineers.

President Low, of the American Society of Mechanical Engineers.

President Kelly, of the American Institute of Mining and Metallurgical Engineers.

President Osgood, of the American Institute of Electrical Engineers.

President Michelson, of the National Academy of Sciences.

Afternoon: Reception by President Ricketts and Mrs. Ricketts.

Evening: Alumni Smoker, Pageant.

OFFICERS OF THE NATIONAL RESEARCH COUNCIL

THE list of officers of the National Research Council for the year 1924–25 is as follows:

Honorory chairman, George E. Hale, honorary director of the Mount Wilson Observatory, Carnegie Institution of Washington, Pasadena, California.

Chairman, Gano Dunn, president of the J. G. White Engineering Corporation, 43 Exchange Place, New York City.

First vice-chairman, A. A. Michelson, president of the National Academy of Sciences; professor of physics, University of Chicago.

Second vice-chairman, Charles D. Walcott, secretary of the Smithsonian Institution.

Third vice-chairman, R. A. Millikan, director of the Norman Bridge Laboratory of Physics, California Institute of Technology, Pasadena.

Fourth vice-chairman, John C. Merriam, president of the Carnegie Institution of Washington, Washington, D. C.

Permanent secretary, Vernon Kellogg, National Research Council, Washington, D. C.

Treasurer, George K. Burgess, treasurer of the National Academy of Sciences; director of the U. S. Bureau of Standards, Washington, D. C.

Assistant secretary, Paul Brockett, assistant secretary in charge of building, National Academy of Sciences, Washington, D. C.

Assistant secretary, Albert L. Barrows, National Research Council, Washington, D. C.

Chairman, Division of Federal Relations, Charles D. Walcott, secretary of the Smithsonian Institution, Washington, D. C.

Chairman, Division of Foreign Relations, R. A. Millikan, director of the Norman Bridge Laboratory of Physics, California Institute of Technology.

Chairman, Division of States Relations, A F. Woods, president of the University of Maryland.

Chairman, Division of Educational Relations, Vernon Kellogg, National Research Council.

Chairman, Division of Engineering and Industrial Research, Frank B. Jewett, vice-president of the Western Electric Company, New York City.

Chairman, Division of Chemistry and Chemistry Technology, James F. Norris, professor of organic chemistry, Massachusetts Institute of Technology; National Research Council.

Chairman, Division of Geology and Geography, David White, senior geologist, U. S. Geological Survey.

Chairman, Division of Medical Sciences, L. Hektoen, professor of pathology, Rush Medical College; director of the John McCormick Institute for Infectious Diseases; National Research Council.

Chairman, Division of Biology and Agriculture, Maynard M. Metcalf, zoologist, Orchard Laboratory; National Research Council.

Chairman, Division of Anthropology and Psychology, R. S. Woodworth, professor of psychology, Columbia University; National Research Council.

Chairman, Division of Physical Sciences, J. S. Ames, dean of the College Faculty, professor of physics, and director of the Physical Laboratory, Johns Hopkins University; National Research Council.

SCIENTIFIC NOTES AND NEWS

THE council of the National Academy of Sciences has accepted the joint invitation of Harvard Univer-

sity and the American Academy of Arts and Sciences to hold the autumn meeting of the National Academy of Sciences in Cambridge and Boston, November 10, 11 and 12, 1924. Arrangements for this meeting will be made as usual by the local committee, the secretary of which is Dr. Edwin B. Wilson, Harvard School of Public Health.

DR. ROBERT A. MILLIKAN, recent recipient of the Nobel award in physics, has been granted the honorary degree of doctor of science by Trinity College, Dublin.

DR. E. S. DANA, professor of mineralogy at Yale University, and Dr. Richard Zsigmondy, professor of inorganic chemistry at Göttingen, have been elected corresponding members of the Vienna Academy of Sciences.

DR. TRUMAN W. BROPHY, of Chicago, who has gone to Luxemburg to attend a meeting of the International Society of Dentistry, of which he is president, was made an officer of the Legion of Honor by the French government on August 1.

THE Moxon Medal of the Royal College of Physicians of London has been awarded to Sir Leonard Rogers, M.D., F.R.S., on the recommendation of the council.

ACCORDING to the *Journal* of the American Medical Association, Senator E. Maragliano, founder of the Maragliano Institute and for nearly fifty years connected with the University of Genoa, was tendered an ovation by friends, scientific societies and state authorities on the occasion of his lecture, on June 28, when he reached the age of retirement. This last lecture was a review of what he and his school have accomplished in the nearly fifty years of his connection with the university and since he founded the Maragliano Institute. A bronze statuette medal and illuminated address were presented to him, and a banquet closed the day.

PROFESSOR H. R. KENWOOD, holder of the Chadwick chair of hygiene at University College, London, will retire next December.

UNDER the new regulations making sixty years the age limit, Drs. Kinnosuke, Miura, W. Okada and Y. Tashiro, of the Tokyo Imperial University, have resigned their professorships.

DR. RAY LYMAN WILBUR, president of Stanford University and former president of the American Medical Association, was appointed permanent chairman of the medical council of the Veterans' Bureau, which closed its first session in Washington, D. C., on July 24.

AMERICANS present at the twenty-first Congress of the Société des Américanistes, which opened in Sweden on August 19, included Dr. Franz Boas, of Columbia University, Dr. R. H. Lowie, of the University of California, Dr. J. W. Fewkes, chief of the Bureau of American Ethnology, and Dr. H. H. Saville, of Columbia University.

PROFESSOR A. W. SMITH, head of the department of chemical engineering in the Case School of Applied Science, Cleveland, has been designated by President L. H. Baekeland to act as the representative of the American Chemical Society on the occasion of the inauguration of Robert Ernest Vinson as president of Western Reserve University and also at the dedication of the new building of the School of Medicine on October 9.

DR. FREDERICK W. ZONS, research chemist at the New Process Gas Mantle Co., has been appointed to head the engineering staff of the General American Radio Corporation as consulting chemical engineer.

CAPTAIN H. P. DOUGLAS has been appointed hydrographer of the British Navy.

ANNOUNCEMENT has been made by the United States Department of Agriculture of several new appointments to field positions in the Research Branch of the Forest Service. These are Mr. R. E. McArdle, of Norfolk, Virginia, to the new Pacific Northwest Forest Experiment Station; Mr. George B. Shivery, of Pennsylvania, to the Southern Forest Experiment Station, at New Orleans, La.; Mr. E. E. Probstfield, of Minnesota, to the Cloquet (Minn.) Forest Experiment Station, and Mr. Lester H. Reineke, of New York, at the Appalachian Forest Experiment Station, Asheville, N. C.

ACCORDING to press dispatches, Captain Knud Rasmussen, the Danish explorer, has arrived at Kotzebu Sound, 150 miles north of Nome, Alaska. Captain Rasmussen left Europe in the summer of 1921 on an expedition to the Arctic regions of which the chief object was the study of the Eskimo, their customs, folk-lore, history, language and religion, and no word has been received from him for fifteen months.

DR. KOTARO HUNDA, director of the metallurgical department at the Imperial University, Tokio, will come to the United States as official representative of the Japanese government at the International Steel Exposition to be held in Boston from September 22 to 26.

PROFESSOR GOESTA FORSELL, Swedish authority on Roentgen-ray theraphy, has been invited to give the memorial lectures on the late Professor Eugene W. Caldwell, the American radiologist, at the Roentgen Congress in Boston, on September 3.

THE Harveian Oration of the Royal College of

Physicians of London for 1925 will be given by Sir Frederick Mott.

DR. JOHN TIMOTHY GERAGHTY, associate professor of urology in the James Buchanan Brady Urological Institute at The Johns Hopkins Hospital, died on August 18 at the age of forty-eight years.

DR. ROBERT GRIER LE CONTE, the distinguished Philadelphia surgeon, died by suicide, on August 6, aged fifty-nine years.

SEYMOUR BOWER, ichthyologist and member of the United States Fish Commission, died on July 25 at the age of sixty-nine years.

DR. DAVID MACFARLAND CASTLE, of Philadelphia, physician and entomologist, died on August 6, aged eighty-one years.

FRANK A. SPRAGG, associate professor of farm crops at the Michigan Agricultural College, Mrs. Spragg, and their youngest son were killed on August 12 by a collision of their automobile with a passenger train.

SIR GEORGE BEILBY, F.R.S., distinguished British industrial chemist, died on August 1 at the age of seventy-three years.

THE Paris correspondent of the *Journal* of the American Medical Association writes that the members of the municipal council of Paris have presented to M. and Mme. Vallery-Radot, the son-in-law and daughter of Pasteur, the first copy of the memorial work published in connection with the celebration of the centenary of the great scientist. The work is from the pen of M. René Weiss, director of the cabinet of the president of the municipal council, to whom the descendants of Pasteur entrusted the valuable documents in their possession.

THE citizens of Albany, N. Y., have subscribed the funds necessary to erect a monumental statue of Professor Joseph Henry, who made the first successful experiments in long distance electrical transmission while he was a teacher in the Albany Academy from 1828 to 1831. The proposed statue will represent Henry as a young man of about thirty engaged in the demonstration of his experiments and it is intended that the figure shall surmount a pedestal bearing reliefs depicting episodes of his career in Albany, the place of his birth. The execution of the work has been entrusted to Mr. John Flanagan, the well-known sculptor of New York City, and the responsible civic body supporting the undertaking is the Albany Institute. It is understood that the money for this monument has been raised by the activities of Dr. John M. Clarke and ex-Governor Martin H. Glynn.

RUSSIAN scientists now living outside of Russia will hold a meeting in Prague, Czechoslovakia, from September 25 to October 2. There will be four sections. Professor P. B. Struve has been appointed chairman of the Section of Jurisprudence and Economy; Professor A. A. Kisewetter, chairman of the Section of Philosophy, History and Philology; Professor M. M. Novikov, chairman of the Section of Natural Sciences and Medicine, and Professor E. L. Zubashev, chairman of the Section of Pure and Applied Mathematics and Technical Sciences. A special session will be in honor of the scientific work of Professors I. P. Pavlov and N. P. Kondakov, both members of the Russian Academy of Sciences, and in commemoration of the recently deceased professors, P. I. Novgorodtzev and N. I. Androusov.

THE joint committee on definitions and standards held its twenty-sixth meeting in the Bureau of Chemistry from August 18 to 22, under the chairmanship of Dr. W. W. Skinner. Proposed standards for ice cream, meat and meat products, wheat flour, jams and jellies were discussed. The joint committee is composed of nine members, three representing the Association of Official Agricultural Chemists, three representing the Association of American Dairy, Food and Drug Officials, and three the United States Department of Agriculture. This committee recommends definitions and standards for food products for the guidance of federal and state officials in the enforcement of food laws.

THE autumn meeting of the Institute of Metals is to be held in London from September 8 to 11. On the first day the third annual autumn lecture will be delivered by W. M. Corse, of the National Research Council, on "Recent developments in non-ferrous metallurgy in the United States, with special reference to nickel and aluminium-bronze." On September 9 the general meeting will be held at the Institution of Mechanical Engineers, and a selection of papers will be presented and discussed. Following luncheon at the Connaught Room, members will visit the British Empire Exhibition. On September 10 the general meeting will be concluded, more papers will be discussed and visits will be paid to various works and to the National Physical Laboratory. On the last day there will be a river trip to Windsor and Eton.

THE sixth session of the International Commission on Illumination was held at Geneva, Switzerland, from July 22 to 25. Dr. E. P. Hyde, director of research at the Nela Park Laboratories, Cleveland, presided, and C. O. Mailloux, Clayton H. Sharp and other American delegates were in attendance. Dr. H. E. Ives, of the Western Electric Company, presented a paper on the adoption of a primary standard of light, and reports were submitted by the French and American committees. Other subjects dealt with by the commission were standards of light suitable for

photographic sensitometers and heterochromatic photometry. K. S. Gibson gave a paper on "The relative visibility function," and a resolution was passed that the commission adopt at the session being held a provisional table of values for this function. A committee was appointed to study all matters relating to colorimetry.

A CHEMICAL exposition showing chemical products of thirty different groups is to be held in Turin, Italy, during the months of September and October of this year under the auspices of several Italian chemical associations.

AN international health congress will be held at Lausanne on August 4, 5 and 6, under the auspices of l'Union Internationale contre la Tuberculose.

A JOINT meeting of the Southern California Section of the American Chemical Society and visiting members of the American Institute of Chemical Engineers was held at the Mary Louise Café, Los Angeles, on August 1.

THE twenty-eighth Congress of Alienists and Neurologists of France and French-speaking countries was held at Brussels, from August 1 to 6, under the chairmanship of Dr. Glorieux, the general inspector of psychopathic hospitals and of the colonies for the insane, in Belgium, and of Dr. Ernest de Massary, physician to the hospitals of Paris.

THE American Philosophical Association has been authorized to convene the next International Congress of Philosophy in the United States during the second week of September, 1926. The place of meeting—to be more definitely announced later—will be at one of the eastern universities, not far from New York. English, French, German, Italian and Spanish will be recognized as the official languages of the Congress. Correspondence may be addressed to the corresponding secretary, Professor John J. Coss, Columbia University.

THE International Conference on Health Problems in Tropical America, which was held at Kingston, Jamaica, by the United Fruit Company, was formerly opened on July 22, when the acting governor of Jamaica, Colonel Bryan, gave the address of welcome. According to the *Journal* of the American Medical Association, George E. Vincent, New York, president of the Rockefeller Foundation, and Dr. William E. Deeks, head of the medical department of the United Fruit Company, also gave addresses. The first day's program included addresses by Dr. Vincent on "International aspects of public health"; Dr. Charles Cassedy Bass, New Orleans, "The relation of the malaria carrier to malaria prevalence"; Dr. Henry Rose Carter, Washington, D. C., "The preferential and compulsory breeding places of some disease-bearing mosquitoes"; Dr. Francis Metcalf Root, "American anopheline mosquitoes and their relation to the transmission of malaria"; Dr. N. P. Macphail, Quirigua, Guatemala, "A report on the use of intramuscular injections of quinin in the treatment of malaria" and Joseph A. LePrince, Memphis, Tenn., "Can we get better anopheles and malarial control at lower cost?" Enroute to Kingston, the delegates visited the Academy of Medicine, Havana, Cuba, where Dr. Frederick G. Banting, Toronto, gave an address, after which a formal reception was held. On visiting the hospitals for lepers on July 22, the delegates were addressed by Sir Leonard Rogers, of London, on "Leprosy."

PROFESSOR K. F. WENCKEBACH recently summoned a conference in Vienna, at which Dr. W. B. Coffey and Dr. P. K. Brown demonstrated the technique of their operation for the relief of angina pectoris, comparing it with the operation performed by Dr. G. Hofer, of Vienna. A plan of further joint investigation was arranged and another meeting proposed for 1925.

ACCORDING to the *British Medical Journal*, a meeting of subscribers to the fund which has been raised in memory of the late Dr. and Mrs. Augustus D. Waller was held at the London School of Medicine for Women, on July 17, under the chairmanship of Sir Edward Sharpley Schafer. Dr. Waller was at one time lecturer in physiology at the London School of Medicine for Women, and Mrs. Waller was first a student, then demonstrator, and later, until her death, a member of the council. It was therefore resolved that the major part of the fund should be devoted to some purpose in connection with that school. The fund collected amounts to £1,911, and it may eventually reach £2,000. It is proposed to earmark the sum of £100 as a contribution to a Waller Memorial Research Laboratory at St. Mary's Hospital, with which Dr. Waller was long connected as lecturer in physiology, if that project materializes. The remainder will be handed over to the council of the London School of Medicine for Women as a trust to be known as the Augustus and Alice Waller Memorial Research Fund. It is intended that the fund shall be used for the purchase of apparatus and materials, and for the provision of mechanical assistance and the publication of results; it is not to be regarded as in the nature of a scholarship or salary. The fund will be administered by the council of the London School of Medicine for Women, with the advice of the school committee.

DR. W. W. CORT, who has been in China during the last year as visiting professor in parasitology at the Peking Union Medical College, will return to

Baltimore about October 1 to take up his work again in the School of Hygiene and Public Health of the Johns Hopkins University. In addition to teaching at the Peking Union Medical College, Dr. Cort, associated with Dr. J. B. Grant and Dr. N. R. Stoll, has been engaged in investigations on hookworm disease in China. Surveys and epidemiologic studies have been carried out at Chefoo, Peking, Wuchang, Soochow, Nantungchow and Canton. The headquarters of the work have been at the Soochow Hospital, Soochow, where a continuous program of experimental researches has been carried out, beginning with July, 1923. The China Hookworm Commission has worked under the auspices of the Peking Union Medical College, and has been financed by the International Health Board of the Rockefeller Foundation.

UNIVERSITY AND EDUCATIONAL NOTES

The department of medicine of the University of Virginia at Charlottesville has received the sum of $15,000 from an anonymous donor to establish scholarships in memory of Dr. Richard H. Whitehead, dean of the school from 1905–1916.

The University of Cambridge has received a bequest from the late Mrs. Constance Jenkinson for the purpose of founding a lectureship for the encouragement and advance of research in comparative and experimental embryology in the university, to be called the John Wilfred Jenkinson Memorial Lectureship, in memory of her husband, a fellow of Exeter College, who was killed in the war.

The Board of Governors of McGill University has authorized the construction of a new building for the department of electricity.

On August 1, the London School of Tropical Medicine became incorporated in the London School of Hygiene and Tropical Medicine under the directorship of Dr. Andrew Balfour. All the members of the old institution will become members of the staff of the new London School of Hygiene and Tropical Medicine.

At the meeting of the Board of Trustees of the University of Mississippi on July 29, Dr. Alfred Hume, vice-chancellor, was elected chancellor; Dr. J. O. Crider, assistant dean of the School of Medicine, was elected dean; Lloyd E. Thatcher, of the department of zoology of the University of Michigan, was elected professor of biology and embryology, and T. E. Wilson, Jr., was elected acting assistant professor of histology and physiology.

At the North Carolina State College of Agriculture and Engineering, Dr. Arthur J. Wilson, of Wabash College, and Dr. Frank E. Rice, of Cornell University, have been appointed professors in the department of chemistry.

Dr. Floyd H. Allport, formerly associate professor of psychology in the University of North Carolina, has accepted a professorship of political and social psychology in the new School of Citizenship and Public Affairs, to be opened this fall at Syracuse University.

Professor E. M. Watson has been appointed lecturer on pathologic chemistry at the Western University Faculty of Medicine, London, Ont., and consulting pathologist for Victoria Hospital.

Professor Ulrich Ebbecke, of Göttingen, has been appointed to the chair of physiology at Bonn, vacated by Professor Hofman.

DISCUSSION AND CORRESPONDENCE

NEW CASTS OF THE PITHECANTHROPUS REMAINS

In the beginning of July, 1923, during the writer's visit to Professor Eugene Dubois, to examine, at the latter's invitation and after their long seclusion, the highly important originals of the *Pithecanthropus*, the need of new and reliable casts of all the remains was urged upon Professor Dubois, who promised to comply as soon as circumstances permitted. On July 10, this year, the following gratifying and self-explanatory letter was received:

"Dear Dr. H.

To-day I have forwarded to the Koninklyke Akademie von Wetenschappen, Amsterdam, casts of all the fossil remains of *Pithecanthropus erectus:* the calvarium, the endocranial cavity, the femur, the three teeth and the mandibular fragment, for the U. S. National Museum, Smithsonian Institution, Washington, D. C.

I beg to excuse the late date of this, a year ago promised sending, by my having been seriously indisposed during a long time and the circumstances that we have no specialist in this country to make casts of this kind, so that the work had to be done for the greatest part by my own hands.

Believe me sincerely yours,
(Sgd.) Eug. Dubois."

It is understood that two other sets of these casts have been made, one of which is destined for the American Museum of Natural History.

Aleš Hrdlička
U. S. National Museum

AS STUDENTS UNDERSTAND IT

I think it was President Eliot who used the expression, "The incredible incapacity of the average student to receive instruction."

During 36 years, 34 of which have been continuous at one institution, of active work in teaching—per-

haps, from what follows, I should say, in trying to teach the biological sciences, one is apt to have had experience with various types of student mentality and to have learned something of the intricate cerebrations of student aspirants to wisdom.

One can expect a certain amount of misspelling of scientific terms, such as "Senterpede; Bile Ducks; Liver fruit (flukes)," and so forth. These will always occur under the present system of teaching spelling in the lower schools.

Looking over a list of choice and rare gems of student misinformation evidenced in written answers, which has been gleaned from actual test papers during a long period, the following actual answers would seem to have been faked, or to be the lucubrations of a disordered imagination.

The following are among the more amazing:

Enzymes are plants having hairs that are inactive; such as cactus and onion.

Root-tubercle bacteria attack the roots, causing them to die, and it is due to the decay of layer or top of layer of plants and vegetable matter that causes the production of fuel.

By metamorphosis is meant the change in form which takes place in animals in whose life history metamorphosis takes place.

Pollination is a process by which the ovary of the stamen is fertilized by the pollen which comes from the *antlers*.

Malaria is caused by a certain kind of mosquito, and in a little while he has yellow fever. Of course every kind of louse does not carry yellow fever.

Sporozoa is a disease caused by certain forms of bacteria.

Birds have one antiseptic kondyle (Occipital condyle).

An antiseptic is something that prevents or stamps out fumigation.

Bacteria are used when vaccinating a person for disease; again they are used in spraying plants.

Vertebrates are mammals or man, such as birds, lizards, reptiles, snakes, fish, whales.

A notochord is an animal that has not a backbone.

Arthropods have the nerve system on the Bellephloem (Belly floor?).

A metamorphosis is a sucking insect and is very injurious to trees.

Placenta is center of some animal element which is surrounded by some more of animal substance not as vital as it.

An insect is a vertebrate and invertebrate animal, having no true back bone.

Liver-flukes attack the tail of the animal, which excited, moves its tail; this is kept up until finally the tail falls off.

Chinch-bugs may be controlled by use of carbon bisulphide gas on the outer rows of a corn field.

Reptiles have two or more pairs of limbs, such as the locust and others.

O Tempora, O Mores!

ELLISON A. SMYTH, JR.

THE SCIENTIST AND AN INTERNATIONAL LANGUAGE

IN the current (June 20) issue of SCIENCE I have noted the communication of Dr. Roland G. Kent on "The scientist and an international language." The need for an international language is great both in science and in other fields. It is perhaps possible to conceive that the translation of articles upon scientific subjects into Latin would be relatively easy for a very few men, but for most of us such a thing would constitute a *tour de force*, in fact a practical impossibility, even assuming that we had at hand an adequate "unabridged" English-Latin dictionary of modern scientific and technical expressions.

To express modern ideas in Latin requires exceedingly ingenious, not to say clumsy, circumlocutions. The technical dictionaries in the vernacular are always far behind the daily and common use of technical and scientific expressions and the best dictionaries contain but a portion of the technical terms. As an example I might cite the fact that nearly half of the 1,200 milling and baking terms which I have compiled are not found in "Webster" or the "Standard."

A Latin glossary is perhaps possible for sciences like botany, and without doubt a commission could translate or transliterate most of our modern chemical terms, but it would not be quite so feasible in the social sciences and would certainly be difficult in the mechanical arts. In high school and university I devoted five years to Latin, one year to Greek and four years to German, also taking a little French and Spanish, yet I should certainly hopelessly fall down if the task were given me to describe in Latin a walk around Lake Calhoun, let alone writing an article on measurement of viscosity or talking to a foreign chemist regarding the specific rotatory power of a soluble carbohydrate.

In scientific work we could not get along without modern scientific equipment such as pyrex and silica glass, dictaphones and audion valves, and it is certainly not in line with progress or convenience to think of going back to antiquated modes of expression even though that could be accomplished. We have gone beyond the Roman notation and adopted the very simple and easier Arabic notation. We have adopted universal musical notation and have nearly come to full use of the metric system. Why should we hesitate to adopt Esperanto, which nearly if not completely possesses every desired quality which an international language should possess?

Dr. Kent asserts that any artificial language can not convey the thought with objective certainty, but that Latin is unsurpassed in this respect. I have for many years made the most practical use of Esperanto in gathering scientific information from non-scien-

tific and scientific men in all quarters of the globe and wish to say that I have found it capable of expressing with exactness shades of meaning which one finds difficult to express in English. The ability of the Greek in this particular is only surpassed by Esperanto with its highly ingenious prefix and suffix system in forming readily understood yet exactly defined expressions.

It was not necessary for me when first I happened on the word "disaudigi" to understand that it meant "to broadcast": *dis*—in different directions, *aud*—hear, *igi*—to cause to. Esperanto has been termed modernized and simplified Latin and "the least common multiple of the European languages." It is not in the true sense an artificial language. Probably 75 per cent. of the roots are of Latin origin, and the very simplicity of the grammar constitutes the best argument for its use as a scientific tool. It is not the words and names that make a language difficult but the grammatical gender, the idiomatic expressions, the similarity of case and verb endings, etc. The grammatical construction of Esperanto is easily mastered by any intelligent person in an hour's study.

Consider for a moment the complications of Latin inflections, for instance, the ending *is* in nouns and adjectives in the dative and ablative plural of the first and second declensions, the genitive singular and many nominative and vocative singulars and accusative plurals of the third declension, occasional genitives in the fourth declension; in verbs many second person singulars and most second person plurals; also a number of adverbs.

The Committee Appointed to Inquire into the Practicability of an International Auxiliary Language of the British Association for the Advancement of Science favored Esperanto and named the disadvantages of Latin. The American Association would do well in its efforts for the advancement of science to follow the lead of the British, French and Italian Associations, the first Pan-American Scientific Congress in 1909, the World Union of International Associations, and numerous other commercial and international organizations and the Central Office of the League of Nations, by endorsing and making use of Esperanto for the purposes for which Dr. Kent proposes Latin.

If difficulties exist they are certainly minor ones which can be overcome, and the point must not be lost sight of that the purpose of an international language is to gain quickly and exactly the information presented by a writer. This will be the more easily possible if the writer expresses his thoughts clearly and simply, and it is a pleasure to assure those who have not used Esperanto that it is an easily used tool of exceeding sharpness and accuracy to which one quickly becomes accustomed. Those who have attended international congresses where Esperanto has been used have always commented on the fluent speech and the obvious understanding which existed, and the smoothness of the transactions in contrast with the tedious proceedings and interruptions for translation at congresses using several national languages.

We might perhaps compare the use of Latin, German and Esperanto in the translation of an article to the comparative pleasure that would be experienced in attempting to drive a wind-broken nag, a 1907 model auto and a 1924 six or eight cylinder coupé on a twenty-five mile trip.

CHARLES H. BRIGGS
MINNEAPOLIS, MINNESOTA

I HAVE seen the letter of Mr. Charles H. Briggs, of Minneapolis, regarding my recent communication on "The scientist and an international language," and desire to make a brief reply.

The difficulty with the use of Latin as the international language for the scientist is not that which is mentioned by Mr. Briggs, but the fact that the budding scientists have not been brought to the study of Latin with the idea that it will in the future be their medium of international communication. If such an attitude had been inculcated, we should see to-day very different results from the study of Latin and should find many more scientists glad to accept the services of the Latin language.

Mr. Briggs's own statement that "probably 75 per cent. of the roots (of Esperanto) are of Latin origin" virtually concedes the case in favor of Latin, in the matter of vocabulary. As for ease of word formation, nearly all the suffixes of Esperanto which form nouns and adjectives, and most of the other formative elements, are taken direct from Latin or from Greek, and are as easily usable in Latin as in Esperanto. It is clear to any one familiar with etymologies that virtually all technical vocabularies in English are of almost exclusively Latin and Greek origin. Probably all of them are, without exception, but from scholarly caution I insert the *virtually*. It happens that I do not know the terminology of milling and baking, but I should be very glad to make an etymological analysis of it, if it should be submitted to me. And while I admit that I could not write in Latin a technical treatise on milling and baking, nor on most other natural scientific subjects, I could not do it in English either. Yet I can see what the Latin would be for the "specific rotatory power of a soluble carbohydrate," since every word is already Latin except the *hydr*, which is Greek and can be used freely in Latin; and as for a walk around Lake Calhoun, I shall be pleased at any time to demonstrate the ease with which it can be described in Latin, if Mr. Briggs will furnish me with the English text: the lake is unknown to me personally.

The other differences between Mr. Briggs and myself are matters of opinion. But in considering them, one must not forget that the Esperantist has almost always approached the study of Esperanto with a considerable previous study of other languages, sufficient to render language study easy to him, and with an enthusiasm raised to a high pitch by repeated assurances that Esperanto is extremely easy. Professor R. A. Muttkowski develops this theme very effectively in *America* for December 30, 1922. But of these two factors, the former is not intrinsic in Esperanto, and the second is extraneously stimulated. Grant the same mental attitude toward Latin or toward any other language as that which has been developed toward Esperanto by its advocates, and the rate of progress would be enormously accelerated. But this is not normal. One may note that Professor Leskien, the great linguist and philologist of Leipzig, found it very difficult to gain a mastery of Esperanto, though he devoted several hours a day to it for three months, and he was a man who spoke a number of modern languages, including several Slavonic languages, which are reputed to be very hard to learn.

ROLAND G. KENT
UNIVERSITY OF PENNSYLVANIA

SCIENTIFIC APPARATUS AND METHODS

ARTIFICIAL CULTIVATION OF FREE-LIVING NEMATODES

THE artificial propagation in pure culture of microscopic organisms, wherever it has been successfully applied, has opened the road to discoveries of the most important and most diversified kinds. The development of cultural methods for the study of bacteria by Pasteur will always stand as one of the important milestones in the progress of bacteriological science. Since Pasteur's time numerous refinements have been made in cultural methods, particularly the introduction of solid media by Koch, and great extensions have been made in the application of this method of study to organisms other than bacteria and fungi. Spirochetes, free-living protozoa, trypanosomes, Leishmaniae, intestinal flagellates and even malarial parasites have been successfully grown in culture, either pure or in conjunction with organisms on which they feed.

So far as I am aware the propagation in pure culture (pure as far as metazoan species are concerned) on artificial media of free-living nematodes has not previously been recorded. I recently made the discovery that certain species of free-living nematodes would thrive and multiply at an astounding rate on ordinary nutrient agar plates. A single isolated adult female of Rhabditis sp., placed on an agar plate with a drop or two of dirty water to supply a bacterial growth, in a period of five days produced hundreds of offspring which swarmed all over the plate. In ten days the offspring numbered many thousands—males, females, eggs and young in all stages of development. The majority of the individuals are found moving about on the surface of the agar, but some burrow into it also. The movements on the agar are sufficiently impeded so that they can be watched after the fashion of a slow-moving picture. The swallowing of bacteria and fungus spores, the excretion of waste matter from the anus, and every detail of locomotion can be observed under ideal conditions. I have succeeded in culturing at least two different species of Rhabditis, a Cephalobus and others which are not positively identified. A pure culture, *i.e.*, a culture containing only one nematode species, seems to develop more rapidly than a mixed culture.

Cultivation of free-living nematodes in this manner suggests a great range of possibilities in the way of study and experimentation, *e.g.*, on foods, effects of hydrogen ion concentrations and of chemical substances, resistance to desiccation, tropisms, effect of various modifications in environment on rate of reproduction and development, etc. In the case of beneficial or injurious species, it might lead to the discovery of methods for controlling or encouraging them. The extremely rapid rate of reproduction and ready inbreeding suggests great possibilities in the way of genetic experiments.

Cultivation on agar plates also furnishes a convenient method of obtaining large quantities of material for taxonomic study, in all stages of development. A drop or two of water washed over the surface of the plate and then placed on a slide with a little ether gives a large number of perfectly clean nematodes for microscopic examination.

For class demonstration the cultivation of the soil nematodes on agar plates is ideal. If a student places a small quantity of soil, especially manured soil, in a piece of gauze or in a fine sieve, and washes it in a beaker of water of about 100° F., for a few minutes, the majority of the nematodes present will fall to the bottom of the beaker. A drop or two of water from the bottom of the beaker is placed on the surface of the agar, the plate is covered and left at room temperature for a week or two and then examined under a microscope. I can guarantee from personal experience that the result will be startling.

Further investigation on the cultivation of these nematodes, especially its application to a larger number of species, had been planned before publishing the work, but an unexpected change in my plans makes it improbable that it can be continued for some

time to come. In order, therefore, that others who are interested in the study of free-living nematodes may pursue the matter further, this preliminary note is published in its present incomplete state.

ASA C. CHANDLER

BIOLOGICAL LABORATORY,
RICE INSTITUTE

SPECIAL ARTICLES

ELECTRIC CONDUCTIVITY OF RED BLOOD CORPUSCLES USING HIGH FREQUENCY ALTERNATING CURRENTS[1]

RUDOLPH HOEBER determined the electric conductivity of suspensions of erythrocytes in isotonic sugar solutions by various substitution methods. He used damped alternating currents of radio frequency for the high frequency currents. Owing to the fact that high frequency apparatus has been very much improved, and it is now possible to obtain undamped alternating currents of any desired frequency, it seemed desirable to make some new determinations. During the past nine months I have spent much time in the attempt to observe a difference, if any exists, between the conductivity of erythrocytes as measured by continuous currents in contrast to that measured at about one thousand cycles per second. It was found that calomel electrodes of large size showed so little polarization during the passage of a small current for fifteen seconds that these could be used for running the current into and out of the erythrocytes. Apparatus was made which reversed the current every fifteen seconds and the final reading was verified during one fifteenth-second interval. The electrode vessels were separated from the erythrocytes by means of agar gel made up with saturated potassium chloride solution. After many methods were tried, a Wheatstone bridge method was finally used. No difference in conductivity with direct current and with a thousand cycles could be established with certainty. Attempts were next made to detect a difference between the conductivity at one thousand and one million cycles. The current of a thousand cycles was generated by a Vreeland oscillator and gave a pure sign wave as shown by the oscillogram. A million cycle current was produced by an electron tube oscillator. This frequency is too great to be studied by the oscillogram, but it is a general opinion of radio engineers that such currents show harmonics. No better source of current, however, was known at this frequency. Measurements made with a bridge whose known resistances were wound according to the Ayrton-Perry winding were very unsatisfactory at a million cycles, although this bridge gave very good results at fifty thousand cycles. Therefore, a very simple and symmetrical bridge was constructed in which the metallic resistances were straight wires and the detector was a crystal detector and sensitive galvanometer. No theoretical defect in this bridge was known, and since no more suitable arrangement has yet been used, the results are taken to be provisionally correct. It was found that the specific conductivity of a sediment of ox-erythrocytes containing a small percentage of serum was 0.001 reciprocal ohms at one thousand cycles per second, and was 0.0014 reciprocal ohms at a million cycles per second.

Hugo Fricke has made some measurements of the capacity reactance of living cells. In order to interpret his data as capacity reactance, certain assumptions had to be made. If it is really true that the conductivity is greater at high frequency and that the cells show capacity reactance, a simple and time-honored picture of a cell which would show these phenomena is one in which the cell interior is a moderately good conductor of electricity but the cell surface acts as a dielectric and insulator. When a direct (continuous) current is passed through a sediment of the cells, the current passes through the film of medium separating the cells and does not pass through the cells themselves to any large extent but when a high frequency alternating current is passed, it passes through the medium as well as before and in addition to that it passes directly through the cells, the insulating surface of each cell acting as the dielectric of a condenser.

These preliminary measurements are published owing to the fact that the work will have to be interrupted during the summer.

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STINGING CRYSTALS IN PLANTS

STINGING crystals are widely distributed throughout the vegetable kingdom. They are in the form of raphides, composed of calcium oxalate, and their action is generally regarded as mechanical. As a matter of fact, however, the mechanical effect of such crystals is not the sole cause of the irritation, though this is a contributing factor. Calcium oxalate in the form of raphides is common particularly in the Monocotyledons, but by no means always do they have stinging properties. Some other factor must be looked for. For the purpose of this investigation the Cabo Negro palm (*Arenga pinnata* Merr.), the dumayaka (*Arenga tremula* Becc.) and the pungapung (*Amorphophallus campanulatus* Blume) were used. In the first two the crystals occur in the fruit in a layer of cells on the inner side of the endocarp;

in the pungapung the crystals occur in the stems and leaves.

Application of the crystals to the skin produces a violent irritation which continues for a considerable period of time. This property is made use of in the Philippines for the protection of fish ponds against robbers. The crushed fruits of Cabo negro are scattered along the edges of the ponds, and make a very effective barrier against bare-footed intruders.

Many of these plants containing stinging crystals are used for food purposes. Prolonged boiling renders them harmless, and microscopic examination shows that the crystals have been destroyed. The irritation produced by the fresh material is very similar to that produced by the latex of the unripe papaya (*Carica papaya* L.), in which the active agent is the proteolytic enzyme papain. This affords a hint as to the reasons why irritation is produced by some plants with raphides, and not with others.

Four possibilities may be taken into account: (1) Irritation may be due to the mechanical action of the crystals; (2) It may be due to organic acids; (3) It may be due to an enzyme; or (4) It may be due to a combination of (1) and (2) or (1) and (3) or a combination of all three.

A strong infusion of the crushed tissue was filtered over a suction pump. The filtrate, though devoid of crystals, was found to produce irritation when left in contact with the skin, but its action was not nearly as violent as when the crystals were present. Scratching of the skin followed by application of the filtrate produced much more comparable results. The conclusion, therefore, is that the crystals are essential to the production of the full amount of irritation, but that the active agent which produces the effect after the first mechanical action of the raphides (which may be reproduced experimentally by pin pricking) is some substance associated with them. This is not an acid, as the liquid is slightly alkaline in the case of the palms and neutral in *Amorphophallus*. In *Laportea* and *Urtica* (*Urticaceae*) it has been shown that the irritation is due to formic acid, injected after the skin has been pierced by the siliceous trichomes. The mechanism in the cases of stinging hairs may, therefore, be compared to that of stinging crystals. Mechanical piercing is followed by the further action of an irritant. Bearing in mind the similarity in sensation produced by these crystals with that produced by the latex of the papaya, some confirmatory experiments were carried out with the result that conclusive proof was produced that the irritant was a proteolytic enzyme. Within little more than an hour cubes of hard-boiled white of egg were appreciably corroded when immersed in the juice. Ammonia and metallic salts (such as mercuric chloride) acting as enzyme inhibitors when added to the juice destroyed its irritating properties for the most part, though the annoying prickling of the raphides could still be felt.

The custom of boiling the tissues of plants containing stinging crystals before using them for food has two objects. First, heating with water dissolves the crystals, and second, the heat destroys the enzyme.

SUMMARY

The results go to show that in the case of plants with stinging crystals, the action consists of two distinct stages: (1) The mechanical action of the raphides in piercing the skin; (2) The entrance through the minute wounds of a proteolytic enzyme which is the cause of the greater part of the effect.

The removal of the crystals by filtration or the destruction of the enzyme will not eliminate all the irritating properties, but the two actions together are sufficient, and so the action must be regarded as being produced by combination of the two factors.

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THE WESTERN SOCIETY OF SOIL MANAGEMENT AND PLANT NUTRITION

THE Western Society of Soil Management and Plant Nutrition held its third annual meeting on June 24 and 25, commencing one day in advance of the regular session of the Pacific Division of the A. A. A. S. Twenty-five members attended and participated freely in the discussion of the papers.

Four half-day sessions and a business meeting were held and the following program was presented:

SOIL ALKALI AND SOIL ACIDITY

Replaceable bases in relation to soil acidity and the theory of replaceable bases: W. P. KELLEY.

The relation of certain alkali salts to the growth of plants: A. R. DAVIS and D. R. HOAGLAND.

Tolerance studies for alkali soils in Idaho: R. E. NEIDIG and H. P. MAGNUSON.

The injurious after-effects of sorghum: J. F. BREAZEALE.

THE SOIL SOLUTION

Nature and promise of the soil solution: J. S. BURD.

Secular and seasonal changes in the soil solution: J. S. BURD and J. C. MARTIN.

Some physiological aspects of soil solution investigations: D. R. HOAGLAND.

Soil structure and the soil solution: M. D. THOMAS.

Replaceable bases in relation to the soil solution: W. P. KELLEY.

PLANT NUTRITION

The stimulation effect of NaCl upon respiration and growth of wheat: A. R. DAVIS and L. J. TEAKLE.